of acute diarrhoea, commonly precedes the development of Guillain-Barré syndrome.[5] There is a close association between axonal Guillain-Barré syndrome and antecedent *C jejuni* infection.[5] The antecedent infectious symptom was diarrhoea in three of five patients with axonal Guillain-Barré syndrome described by Feasby *et al*.[3] Observations by Griffin *et al*[4] confirmed that AMSAN follows *C jejuni* infection. Serum samples from patients with axonal Guillain-Barré syndrome subsequent to *C jejuni* enteritis often have IgG class autoantibodies to gangliosides GM1, GM1b, GD1a, or GalNAc-GD1a in the acute phase of the illness,[6] and there is molecular mimicry between these gangliosides and the lipopolysaccharides of *C jejuni* isolates from patients with Guillain-Barré syndrome.[6] This ganglioside mimicry may trigger high production of the IgG antiganglioside antibodies, and these autoantibodies may cause motor nerve dysfunction in patients with GBS.

Interestingly, Hagensee *et al*[7] reported a case of *"C jejuni* bacteremia and subsequent Guillain-Barré syndrome" that occurred in a patient with chronic graft versus host disease after allogenic bone marrow transplantation. Because there was acute flaccid paralysis associated with sepsis, some physicians might have diagnosed critical illness polyneuropathy. Conversely, the existence of this case strongly suggests that some diagnoses of critical illness polyneuropathy should actually be axonal Guillain-Barré syndrome or AMSAN. Our hypothesis of the nosological relation between critical illness polyneuropathy and axonal Guillain-Barré syndrome is shown in the figure. Serum IgG antibodies against GM1, GM1b, GD1a, or GalNAc-GD1a could be used as immunological markers for axonal Guillain-Barré syndrome.[6] To examine the aetiology of critical illness polyneuropathy and its nosological relation to axonal Guillain-Barré syndrome, it is necessary to investigate whether patients with critical illness polyneuropathy have antiganglioside antibodies during the acute phase of the illness.

NOBUHIRO YUKI
KOICHI HIRATA
Department of Neurology,
Dokkyo University School of Medicine, Japan

Correspondence to: Dr Nobuhiro Yuki, Department of Neurology, Dokkyo University School of Medicine, Kitakobayashi 880, Mibu, Shimotsuga, Tochigi 321–0293, Japan.

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Repetitive transcranial magnetic stimulation in the treatment of chronic negative schizophrenia: a pilot study

Recently, a new technology known as repetitive transcranial magnetic stimulation (RTMS) has been developed.[1] In 1994, the use of magnetic stimulation in clinical psychiatry was suggested.[2] Since then, it has been used in the study or treatment of obsessive-compulsive disorder, conversion disorder, schizophrenia, and particularly, depression.[3]

Our pilot study aimed to assess the possible adverse effects of this treatment in chronic schizophrenic patients with severe negative symptoms; to evaluate if direct RTMS of the prefrontal cortex might improve negative symptoms or cognitive impairments[4] in patients with chronic schizophrenia; and thirdly, to note if RTMS might modify the deficit in prefrontal cortical activity, often referred to as hypofrontality, long established in schizophrenia,[5] specially under conditions of task activation.

Six right handed patients with chronic schizophrenia were identified at the outpatient psychiatric service of the Hospital Clínic of Barcelona. There were two men and four women (mean age 39).

Exclusion criteria included alcohol or substance abuse dependence disorder in the past 5 years, focal neurological findings, systemic neurological illness, taking cerebral metabolic activator or vasodilator medications, electroconvulsive therapy within 6 months, and significant abnormal findings on laboratory examination.

All patients were taking neuroleptic drugs, but a stable dose for at least 3 months was required. All patients were studied off benzodiazepines for at least 1 week before beginning the treatment. During the RTMS, psychotropic medications were continued at the initial dosage.

All patients were admitted to hospital. Inpatients underwent the UKU side effects scale,[6] the positive and negative syndrome scale (PANSS), and a neuropsychological battery, the day before beginning the treatment and at the end of the treatment. The UKU scale was also administered after each session.

An equivalent neuropsychological battery was used on both occasions, which consisted of the block design subtest of the Wechsler adult intelligence scale, the trail making tests A and B, the FAS verbal fluency test, and two subtests of the Wechsler memory scale (the visual memory reproduction and the verbal paired associates subtests).

A brain SPECT study was performed using a rotating dual head gamma camera, fitted with high resolution fanbeam collimators. Two ^{99m}Tc-HMPAO SPECT scans with cognitive activation, such as the Wisconsin card sorting test (WCST), were performed on each patient (24 hours before the beginning of the treatment and 24 hours after the last session).

RTMS was given with a Mag Pro magnetic stimulator, 5 days a week, during 2 weeks, at a dosage of 20 Hz for 2 seconds, once per minute for 20 minutes at 80% motor threshold. The motor threshold was determined by visualisation of finger movement. A butterfly magnetic coil was placed tangential to the orbital area, on the C_3 and C_4 EEG point.

An important finding of this study was that RTMS may be given to stable schizophrenic patients without exacerbating their psychoses. All patients tolerated the RTMS well, with minimal side effects (mild headache and tinnitus).

Table Neuropsychological tests and PANSS scores

Test		*Mean (SD)*	
Block design	Pre	49 (11.95)	NS
	Post	50 (8.69)	
Trail making test A	Pre	38.3 (9.83)	NS
	Post	42.6 (14.1)	
Trail making test B	Pre	38.3 (4.5)	NS
	Post	41 (10.03)	
Inmediate visual reproduction	Pre	50.5 (4.82)	NS
	Post	54.8 (11.2)	
Delayed visual reproduction	Pre	46.19 (8.23)	p<0.05
	Post	53.8 (12.64)	
Inmediate verbal paired associates	Pre	54 (7.46)	NS
	Post	59.5 (10.03)	
Delayed verbal paired associates	Pre	8.8 (1.1)	NS.
	Post	8.8 (1.17)	
PANSS-PG	Pre	37.67 (11.15)	NS
	Post	36.5 (11.47)	
PANSS-N	Pre	31.67 (8.26)	p<0.02
	Post	27.83 (8.47)	
PANSS-P	Pre	16.83 (7.28)	NS
	Post	15.33 /7.55)	

Pre=pretreatment; Post=post-treatment; PANSS= positive and negative syndrome scale; PG=general psychopathology scale; N=negative scale; P=positive scale.

Initial SPECT of one patient was reported to be normal, showing no evidence of hypofrontality. The remainder of the patients showed hypofrontality on the initial neuroimaging. The results after RTMS indicated no change in the hypofrontality.

Negative symptoms showed a general decrease for all patients (table). Significance ($p<0.02$) was noted on the PANSS negative symptoms subscale. These patients seemed to be more sociable than when originally seen. Nevertheless, clinical effects of the RTMS were subtle and difficult to distinguish from those derived from the supportive environment of the psychiatric ward.

With regard to the neuropsychological battery, we found a general improvement in all post-treatment scores (table), but only delayed visual memory achieved significance ($p<0.05$). This feature might be basically explained by improvement of attention, specifically of the maintenance of attention, which allows the correct function of the working memory. Thus, although there are methodological limitations regarding the power of our conclusions, it is certain that there has been an improvement in the attentional capability.

We found that all patients (except one, who was always within the normal range) diminished their number of perseverative answers and errors on WCST (items characteristically altered in schizophrenia) after the RTMS. However, significance was not achieved on any WCST scores.

Two patients who initially did not perform any categories on WCST, after the treatment, achieved one category, a possible indication of improvement of their abstract thinking. This change leads us to consider a research strategy previously reported, in which the WCST is used as a screening test for selecting schizophrenic patients. Those initially achieving low category scores would be compared to higher category scorers in an effort to identify a subgroup most likely to benefit from RTMS.

Taking into account these mild improvements together, and the lack of changes in

hypofrontality after treatment, we are considering extending the treatment course to 20 sessions, each at 30 Hz for 1 second, at 90% of motor threshold. It was also suggested that other positions of the coil and other kinds of coils might give better results.

The clinical change in our cohort after the RTMS could be attributed to both the treatment and the supportive environment of the psychiatric ward, and even to enhance compliance to medication during hospital admission. We are aware that the small sample size and lack of controls compel a very careful interpretation of the results. Nevertheless, in the light of these, we suggest further controlled studies of the efficacy of RTMS in negative symptoms of schizophrenia, not only as an add on technique but also as a sole therapeutic procedure. Research on RTMS also requires some controlled studies aimed to the complexity of the methodology (dosage, duration, and localisation), as this form of intervention may prove to be an economical and convenient therapy in treating several psychiatric disorders.

E COHEN
M BERNARDO
J MASANA
F J ARRUFAT
V NAVARRO
Department of Psychiatry

J VALLS-SOLÉ
Department of Neurophysiology

T BOGET
N BARRANTES
S CATARINEU
M FONT
Department of Psychology

F J LOMEÑA
Department of Nuclear Medicine, Institut d'Investigacions Biomédiques August Pi i Sunyer, Hospital Clínic i Provincial. Universitat de Barcelona, Spain

Correspondence to: Dr M Bernardo, Servicio de Psiquiatría, Hospital Clínic i Provincial, Villarroel 170, 08036 Barcelona, Spain. Telephone 00343 2275400, ext 2405; fax 00 343 2275477; email bernardo@medicina.ub.es

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CORRESPONDENCE

Sensory alien hand syndrome

The case report by Ay *et al*[1] of alien hand syndrome and review of the literature neglected the intriguing issue of why in every case so far reported the patient seems to be terrified of the alien limb. Not believing that you are any more in control of a limb is not likely to be a pleasant experience.

Those with alien hand syndrome seem to jump to extremely negative conclusions concerning the intent of the limb. Typically, as in the report of Ay *et al*, the common belief is that the limb has deeply malevolent intentions towards the victim.

It is this aspect of alien hand syndrome that I suggest also needs incorporating into its neurological explanations, and which provides a clue as to why our everyday experience of being in charge of our bodies, and so initiating all personal action, itself has a neurological basis. In other words, while the brain is the seat of all our actions and experiences, there is also a part of our nervous system which is responsible for our belief that we have free will over our behaviour. Patients with alien hand syndrome think that they are no longer in control of a limb because the part of the brain that gives us the sensation of control over our bodies has been damaged. When that happens, our limbs seem to act independently of us.

Research[2] conducted in the 1980s has found that the same electrical brain wave changes that characteristically precede all limb movements, occur several 100 ms before we seem to consciously decide to move a limb. If our conscious decision to act is preceded by brain changes that anticipate action, then our "decision" to choose how to behave or "freedom", as in free will, is in fact illusory. Our choices have in a sense been decided beforehand by our brains.

Spence[3] asserts that evidence such as this, combined with phenomena such as alien hand syndrome, means that philosophers have to reconsider whether we have free will. He argues that these data suggest that our sense of agency is illusory and it follows that most of us share in common the useful delusion that we have free will. Patients with alien hand syndrome have lost this experience in relation to a particular limb. There is a sense then that those who experience the syndrome are closer to the reality of how much we are responsible for our actions than the rest of us. This is because they have lost the function of the part of the brain that normally works to make us think that we have conscious freedom of will. They develop the experience, therefore, of becoming mere remote spectators to the actions of their bodies.

Defenders of human "free will" argue what happens before the brain itself decides to act is still unknown, and there may be a role for our own autonomy there. But even these free will guardians concede the neurological research indicates that whatever happens before the brain is roused, must occur below our conscious awareness.

Yet in alien hand syndrome the patient thinks that the hand has hostile motivations; it is invariably the case that the patient not only thinks that the limb is "not self" but finds that the limb behaves towards the self in a destructive and aggressive manner. This could be explained by the suggestion that if we lose our conscious sense of voluntary control over our bodies, our minds have to come up with an explanation for the location of action of our movements. We decide that if ourselves are not in control, then someone or something else must be; therefore, we no longer have a sense of the limb belonging to us.

Because to lose control over our bodies is one of the most terrifying experiences, our attempt to explain this finding occurs in the context of fear. It may be that our apprehension leads us to misinterpret innocent reflexive acts of our hands, such as scratching or rubbing, as malevolently inspired. Plus it could be that our interpretation of spiteful possession in turn inspires the hand itself, only this is beyond our conscious awareness.

It may therefore be that we need to believe in our own free will and personal control over our acts, because if we did not, we might find the experience of our bodies acting as if we merely came along for the ride, too frightening. Also, we may no longer believe that our bodies or its relevant parts belong to us. All neurologists who have reported alien hand syndrome remark on how psychologically disturbing the symptom is for the patient. Psychiatrists would be interested in the parallels between alien hand syndrome and the "passivity phenomena" of schizophrenia, plus the fact that the two diseases may share corpus callosum pathology,[4] could go some way to explaining why schizophrenic symptoms are frightening to the patient. So it seems we know that our limbs belong to us because they obey us. When they seem to stop responding to our wills, we conclude that our limbs are no longer our own, and try to fend them off. Hence it would seem that one of the prices we had to pay for conscious awareness of ourselves to evolve as a function of the brain, is the delusion that we are responsible for all our actions. If we had conscious awareness of ourselves, but no sense of free will, our bodies would feel alien to us. The philosophical importance of alien hand syndrome is that it shows emphatically via neurology that it is possible to drive a wedge between consciousness and the experience of free will. The brain had to develop the sensation of free will after developing consciousness, because being without the sensation of free will produces extremely negative emotional experiences. So the fact that every case so far reported of alien hand syndrome imputes negative intent to the alien limb might not be an incidental finding, but a core aspect of the disorder.

R PERSAUD
The Maudsley Hospital, Croydon Mental Health Services, Westways Rehabilitation Unit, 49 St James's Road, West Croydon, Surrey CR9 2RR, UK. Telephone 0044 181 700 8512; fax 0044 181 700 8504; email rajendra@btinternet.com

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The authors reply:

We appreciate Persaud's comments regarding the alien hand syndrome, "the perceived malevolence of the affected limb towards its victim, and the question of whether with loss of the conscious sense of voluntary control over our bodies, our minds... decide that if ourselves are not in control then someone or something else must be". We would offer that the value of our particular case is that it was due to a central deafferentation—therefore the term "sensory alien hand syndrome". As